

CONDITIONAL PETITION FOR EXTENSION OF TIME

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefor. The Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

With respect to the restriction requirement, Applicants acknowledge with appreciation the Examiner's indication that Groups I and IV have been rejoined. With respect to the Examiner's rationale for maintaining the restriction requirement as to the remaining groups, the search burden on the Examiner remains unclear. The Examiner indicates that he must consider the different method steps and searches, but main claim 1, for instance, recites the single step of "stably integrating an expression vector comprising a short hairpin RNA (shRNA) construct under control of a ubiquitous promoter into a polymerase II dependent locus of the genome of the non-human vertebrate, of the tissue culture or of the cells of the cell culture." Further, it would seem that it would not occasion a serious search burden to determine whether this step has been performed in tissue culture or cell culture in addition to the elected non-human vertebrate. Therefore, Applicants, again, respectfully request that the Examiner reconsider and withdraw the restriction requirement.

The claims were objected to for certain informalities. In response, Applicants respectfully request that this objection be held in abeyance until the issue of the restriction requirement is resolved.

Applicants' claim for foreign priority was acknowledged, but it was noted that Applicants had not filed a certified copy of the priority application. In response, Applicants will shortly

submit the certified copy under separate cover.

Claims 1-27 were rejected under 35 USC § 101 as being directed to non-statutory subject matter. In response, Applicants have limited "vertebrate" to "non-human vertebrate."

Claims 2-4, 6, 9, 12, 14, 15, 18 and 27 were rejected under 35 USC § 112, second paragraph, as being indefinite. In response, Applicants have amended the claims in a manner which Applicants believe overcomes each of the Examiner's concerns. Thus, in claim 27, Applicants have deleted the word "preferably." In claims 6, 9 and 12, Applicants have deleted the word "etc." In claims 2-4, 15 and 18, Applicants have deleted the word "suitable."

Claims 1-27 were rejected under 35 USC § 112, first paragraph, as being broader than the enabling disclosure.

Claims 1-27 were rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement.

In response to both the lack of enablement and lack of written description rejections, Applicants point out that the claims have been limited to *non-human* vertebrates, and stable integration into *a polymerase II dependent locus* of the genome of the vertebrate. As such the claims are drastically narrowed, and Applicants submit there is adequate enablement and written description to support the narrowed claims.

Claims 1, 2, 7-9, 13, 14, 27 and 30 were rejected under 35 USC § 102(b) as being anticipated by McCaffrey et al. ("McCaffrey"), *Nature*, 418: 38-39 (2002). In response,

Applicants would remind the Examiner that anticipation requires that each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference, and, further, the absence in the prior art reference of even a single one of the claim elements is sufficient to negate anticipation. *In re Robertson*, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Applicants point out that the rejected claim incorporates the substance of previous claim 4, which was not subject to this rejection. Therefore, Applicants believe this rejection should be reconsidered and withdrawn. Applicants also point out that the instant claims require that the expression vector be “stably integrated” into the genome of the non-human vertebrate, or cells in the tissue or cell cultures. McCaffrey injected a shRNA construct into the tail vein of mice. As discussed in the instant specification in the last paragraph on page 1, the approach is well known to lead to only a transient effect lasting only a few days. Consequently, McCaffrey does not teach a stable integration, as required by the instant claims. Therefore, McCaffrey does not anticipate the present claims.

Claim 30 was rejected under 35 USC § 102(a) as being anticipated by Paddison et al. (“Paddison”), *Gene & Development*, 16: 948-958 (2002). In response, Applicants point out that the rejected claim incorporates the substance of previous claim 4, which was not subject to this rejection. Therefore, Applicants believe this rejection should be reconsidered and withdrawn. Applicants also point out that Paddison is also discussed in the instant specification, in the middle of page 2. Paddison integrates shRNA constructs into the genome of cultivated cell lines by random integration. This has the consequence that shRNA expression is observed in variable levels and patterns, and the expressed amount is not predictable. Moreover, the results of this random integration do not allow the extrapolation of the activity of the constructs for in vivo

utilites. Consequently, Paddison does not anticipate claim 30.

Claims 1, 2, 7-11, 13, 14, 24-27 and 30 were rejected under 35 USC § 102(e) as being anticipated by Beach et al. ("Beach"), US 2003/0084471. In response, Applicants point out that the rejected claims all incorporate the substance of previous claim 4, which was not subject to this rejection. Therefore, Applicants believe this rejection should be reconsidered and withdrawn. Applicants also point out that Beach describes the general use of double-strand RNA molecules or RNA interference and the use of shRNA in transgenic animals. However, Beach does not teach persons skilled in the art how these shRNA constructs can be integrated into the genome of the animals. Consequently, Beach does not teach or render obvious the rejected claims.

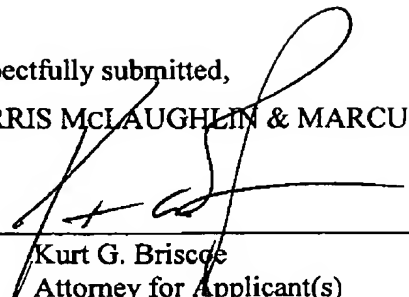
Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
NORRIS MCLAUGHLIN & MARCUS, P.A.

By



Kurt G. Briscoe
Attorney for Applicant(s)
Reg. No. 33,141
875 Third Avenue
18th Floor
New York, New York 10022
Phone: (212) 808-0700
Fax: (212) 808-0844